REMARKS

STATUS OF CLAIMS

Please cancel claims 2 and 26-32 and add new claims 33-37. Also, please amend claims 1, 14, 16, 18, 23 and 25. After entry of this amendment, claims 1, 3-25, and 33-37 will be pending. Support for the amendments can be found throughout the specification and originally filed claims (*e.g.*, US 2006/0251693, pp. 1-2, para. [0012], p. 2, para. [0015], [0020] and [0021], p. 4, para. [0051] and in original claims 2, 14, 16 and 23). No new matter has been added. With the cancellation of claims 2 and 26-32, it is respectfully submitted that no additional claims fees are required for new claims 33-37.

REJECTION UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claim 14 stands rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. In light of the amendment of claim 14 to a single range, Applicants believe that the claimed subject matter is clearly defined. It is respectfully submitted that claim 14, as amended, is in accord with 35 U.S.C. §112.

35 U.S.C. §103 REJECTION

Claims 1-20 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Short (Short *et al.* in WO 01/31339 A1; published May 3, 2001) in view of Mori (Mori *et al.* in U.S. Patent 5,053,398; published October 1, 1991), Hu (Hu *et al.* in U.S. Patent 4,865,870; published September 12, 1989) and Keogh (Keogh *et al.* in U.S. Patent 5,925,552; published July 10, 1999).

Short discloses plasma polymerization of surfaces to which molecules may bind and be assayed for use in the detection and/or activity of a biological molecule bound thereto. It is alleged that Short teaches that the plasma coated surface of the assay product "may be contacted with a broad range of

compounds including agonists and antagonists (p. 6, ll. 4-8 and claim 6)." See Office Action mailed March 19, 2009, p. 4, last paragraph, second sentence. However, although the assay product may be used to identify potential antagonists, Short does not indicate that the polymer coated surface of the assay product is contacted with antagonist. (See, e.g., p. 6, ll. 4-7, the "invention is used to identify" potential antagonists or agonists). For example, the potential antagonists could be identified without contacting a surface by an immunoassay which is a "sandwich" enzyme-linked immunosorbent assay (ELISA) whereby a capture antibody (*i.e.*, a protein) is contacted with the polymer coated surface and the bound capture antibody is contacted with the potential antagonist followed by binding of a detecting antibody resulting in subsequent identification of the potential antagonist. The process of identifying potential antagonists does not require contact between the antagonists and the polymer coated surface.

Claim 1 requires the step of: "contacting said plasma polymer coated surface with at least one type of biologically active carbohydrate molecule". Although Short discloses identifying potential antagonists, there is no disclosure of contacting a plasma polymer coated surface with at least one type of biologically active carbohydrate molecule. See, MPEP §2112(IV) ("The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic."). Moreover, Short only discloses that the biological molecule bound to the plasma polymer coated surface may be a polypeptide or nucleic acid. Nowhere does Short exemplify a nucleic acid bound to such surface. Moreover, nowhere does Short disclose or suggest that the nucleic acid is biologically active or that the nucleic acid is bound to the plasma polymerization treated surface through passive adsorption, as set forth in claim 1. In addition, Short discloses specific examples of the polypeptide as collagen and vitronectin. (P. 7, ll. 1-4; p. 12, l. 27 – p. 13, l. 12). There is no disclosure that either the collagen or vitronectin is immobilized so the carbohydrate molecule is passively absorbed such that the carbohydrate molecule retains its biological activity, as set forth in claim 1. Furthermore, no incubation is

disclosed with the collagen example. Thus, Short neither discloses nor suggests the presently claimed invention.

Mori discloses sulfated homopolysaccharides with anti-HIV activity. It appears that the Examiner relied on Mori. However, Mori does not disclose or suggest immobilization of such homopolysaccharides, and, thus, does not overcome the deficiencies noted above of Short.

At p. 7 of the Office action, the Examiner asserted:

> Therefore, using the guidance provided by the method of Short to provide polymer modified surfaces that may immobilize a wide variety of compounds (including antagonists), the teachings of Hu and Keogh regarding the importance of biologically active carbohydrates and immobilizing them in their native form, it would have been *prima facie* obvious to one of ordinary skill in the art, at the time the invention was made to use the guidance and motivation from the above references to arrive at the claimed invention with an expectation of success.

Although the background of Keogh teaches that in some cases, covalent coupling is not desirable and that ionic coupling is advantageous, Keogh specifically discloses methods of attaching a biomolecule to a medical device surface by using tridodecyl methylaminonium chloride (TDMAC). (Col. 2, ll. 35-39). In addition, Keogh discloses different coatings for ionically bonding heparin. (Col. 2, l. 40 – col. 3, l. 21). Keogh also discloses using a chemical bond to couple a biomolecule. (See, Abstract). However, nowhere in Keogh is there reference to a plasma polymer coated surface, as set forth in claim 1. Prior art must be enabling to be relied upon in an obviousness rejection. (See, MPEP §2141.01(II) and MPEP §2121). Although Keogh discusses various surfaces for binding to a biomolecule, there is no disclosure of a plasma polymer coated surface. Keogh would not have been able to write claims, for lack of enablement and disclosure, directed to plasma polymer coated surfaces.

There is no basis to modify Short to couple a carbohydrate molecule in the form of heparin to a plasma polymer coated surfaced based on Keogh. Any combination of Short and Keogh would result in the use of one or more of the coatings (e.g., TDMAC) set forth in Keogh with the surface of Short. There is no basis to have direct contact or coupling to a plasma polymer coated surface.

Hu discloses a specific method for heparinizing a polymeric substrate. Specifically, Hu's method first requires applying a coating of ammonium salt at an alkaline pH to a polymeric substrate to form a surface active agent. The coated polymeric substrate is then contacted with a solution of a salt of heparin whereby the heparin reacts with the surface active agent of the coated substrate to give a heparinized substrate. Unlike the presently claimed invention, the polymeric substrate of Hu has an additional coating (i.e., the surface active agent formed by ammonium salt). Thus, in Hu, the carbohydrate molecule does not contact the surface of the polymeric substrate comprising amine groups but rather the surface of the surface active agent coated substrate.

In addition, nowhere does Hu disclose or suggest using plasma polymerization alone to produce a coating amenable for passive heparin attachment. Rather, plasma polymerization is merely described as an optional means, not essential to the method of the invention disclosed therein, to prepare the substrate prior to steeping with ammonium salt. (See Hu, col. 6, ll. 51-59). Consequently, if anything, Hu teaches away from the present invention as it requires a surface active agent (i.e., formed by ammonium salt) to bind heparin. Even if the teachings of Hu were combined with Short, and for the sake of argument (though no motivation is present) omitted the steeping step with ammonium salt, one of skill in the art would not have a reasonable expectation of success in achieving passive adsorption of heparin to the polymerized substrate.

In view of the foregoing, it is respectfully submitted that claim 1, along with dependent claims 2-19, are patentable over Short, Mori, Hu and Keogh, each taken alone or in combination.

Claim 21 stands rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Short (Short *et al.* in WO 01/31339 A1; published May 3, 2001) in view of Mori (Mori *et al.* in U.S. Patent 5,053,398; published October 1, 1991), Hu (Hu *et al.* in U.S. Patent 4,865,870; published September 12, 1989) and Keogh (Keogh *et al.* in U.S. Patent 5,925,552; published July 10, 1999) as applied to claims 1-20 above, and further in view of Nilsson (Nilsson et al. in US 2001/0017270, published August 31, 2001). The Examiner admitted that the "Short, Mori, Hu and Keogh references do not teach the limitations of instant claim 21 in which the surface of instant claim 1 is part of a biosensor" (see Office Action mailed March 19, 2009, p. 8, last paragraph). The Examiner relied on Nilsson for allegedly overcoming this deficiency.

Nilsson refers to a biosensor in which a carbohydrate or a derivative thereof is bound to a surface of the biosensor *via* a chemical bond or adsorption. In particular, Nilsson states "the surface of the biosensor can be, for example a gold surface or a modified gold surface, a plastic surface which has been modified with a gold surface, silver surface or another metallic surface, or modifications thereof with polymers to which **chemical coupling** of carbohydrate can be carried out." (Emphasis added, see Nilsson, page 3, para. [0041]). However, nowhere does Nilsson describe any modifications to a plasma polymer surface for passive adsorption of a carbohydrate. Likewise, nowhere does Nilsson exemplify a biosensor with a polymer surface. Rather, Nilsson exemplifies the following:

a) binding of digalactoside with aglycon (*i.e.*, Galα1-4Galβ-OEtSEtCONHNH$_2$) to a silica surface coated with a gold layer modified with mercaptopropionic acid
b) binding of Galα1-4GalβOCH$_2$CH$_2$SCH$_2$C(O)-NHNH -BSA to a silica surface coated with a gold layer modified with mercaptopropionic acid

c) binding of Galα1-4Galβ-BSA to a silica surface coated with a gold layer (not pretreated with mercaptopropionic acid)

Thus, Nilsson only exemplifies biosensors with a surface coated with a gold layer. Notably, in two of the three examples, specifically (a) and (b), the carbohydrate derivatives are chemically coupled to the gold surface. Accordingly, Nilsson does not overcome the deficiencies noted above of Short, Mori, Hu and Keogh. It is respectfully submitted that claim 21 is patentable over Short, Mori, Hu, Keogh and Nilsson, each taken alone or in combination.

Claim 22 stands rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Short (Short *et al.* in WO 01/31339 A1; published May 3, 2001) in view of Mori (Mori *et al.* in U.S. Patent 5,053,398; published October 1, 1991), Hu (Hu *et al.* in U.S. Patent 4,865,870; published September 12, 1989) and Keogh (Keogh *et al.* in U.S. Patent 5,925,552; published July 10, 1999) as applied to claims 1-20 above, and further in view of Dinh (Dinh et al. in U.S. Patent 5,554,182, published September 10, 1996). The Examiner admitted that the "Short, Mori, Hu and Keogh references do not teach the limitations of instant claim 22 in which the surface of instant claim 1 is part of a therapeutic vehicle" (see Office Action mailed March 19, 2009, p. 10, 4th para.). The Examiner relied on Dinh for allegedly overcoming this deficiency.

Dinh teaches a method for preventing restenosis in a stent. In particular, the methods therein describe heparin as being: (i) applied to a fibrin coated stent; (ii) added to a composition of fibrinogen and thrombin before it is completely polymerized on a stent; or (iii) included in the initial mixture of fibrinogen and thrombin applied to a stent so long as the presence of heparin does not lead to a weak fibrin film (see Dinh, col. 8, ll. 30-67). Dinh does not disclose the use of plasma polymerized surfaces. Accordingly, Dinh does not overcome the deficiencies noted above of Short, Mori, Hu and Keogh. It is respectfully submitted that claim 21 is patentable

over Short, Mori, Hu, Keogh and Dinh, each taken alone or in combination.

Claim 23 stands rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Short (Short *et al.* in WO 01/31339 A1; published May 3, 2001) in view of Mori (Mori *et al.* in U.S. Patent 5,053,398; published October 1, 1991), Hu (Hu *et al.* in U.S. Patent 4,865,870; published September 12, 1989) and Keogh (Keogh *et al.* in U.S. Patent 5,925,552; published July 10, 1999) as applied to claims 1-20 above, and further in view of Earhart (Earhart et al. in U.S. Patent 6,077,232, published June 20, 2000). The Examiner admitted that the "Short, Mori, Hu and Keogh references do not teach the limitations of instant claim 23 in which the surface of instant claim 1 is part of a biological sample collection device" (see Office Action mailed March 19, 2009, p. 12, 2nd para.). The Examiner relied on Earhart for allegedly overcoming this deficiency.

Earhart teaches a blood collection device containing an anticoagulant composition. Specifically, Earhart states that,

> The anticoagulant composition is a **soluvated** non-aqueous **solution** comprising a proteinase inhibitor such as for example but not limited to a polysaccharide sulfuric acid ester such as for example heparin. The composition also comprises a blend of one or more alcohols such as for example one or more polyhydric alcohols selected from the group consisting of C1-12 diols such as glycols and derivatives thereof such as for example ethylene glycol or propylene glycol wherein ethylene glycol is preferred for increased solubility and C1-12 polyalkyl diols such as for example polyethylene glycol, polyproplylene glycol or polybutylene glycol wherein polyethylene glycol is preferred for increased solubility and for ready plasticization of the proteinase inhibitor.

(Col. 2, l. 62 – col. 3, l.8).

Furthermore, Earhart states that "the subject anticoagulant composition is placed within the syringe barrel in a liquid state...and remains in the syringe barrel during blood collection due to its movement within the barrel without expulsion thereof." (Col. 1, l. 62 to col. 2, l. 6). Thus,

the anticoagulant composition is not immobilized to the surface but rather in a liquid state that freely moves. In fact, Earhart further emphasizes that, "The alcohol which is preferably polyethylene glycol, combined with the proteinase inhibitor which is preferably heparin, prevents the proteinase inhibitor from drying into an unsoluvated state. Heparin in an unsoluvated state dissolves with difficulty and thus requires more time to disperse throughout a collected blood sample." (Col. 2, ll. 15-21). In fact, Earhart points out that "the use of the anticoagulant composition of the present invention within a blood collection device reduces the anticoagulant solution dispersal time compared to that of dried unsoluvated heparin within a blood collection device so as to be more effective in preventing coagulation within a collected blood sample." Thus, the proteinase inhibitor, heparin, is preferably a liquid which disperses readily throughout a blood sample collected in the blood collection device. Nowhere does Earhart disclose or suggest immobilizing heparin.

Without immobilization, it is respectfully submitted that Earhart does not overcome the deficiencies noted above of Short, Mori, Hu and Keogh. It is respectfully submitted that claim 23 is patentable over Short, Mori, Hu, Keogh and Earhart, each taken alone or in combination.

Claim 24 stands rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Short (Short *et al.* in WO 01/31339 A1; published May 3, 2001) in view of Mori (Mori *et al.* in U.S. Patent 5,053,398; published October 1, 1991), Hu (Hu *et al.* in U.S. Patent 4,865,870; published September 12, 1989) and Keogh (Keogh *et al.* in U.S. Patent 5,925,552; published July 10, 1999) as applied to claims 1-20 above, and further in view of Brigstock (Brigstock et al. in US 2001/007019, published July 5, 2001). The Examiner admitted that the "Short, Mori, Hu and Keogh references do not teach the limitations of instant claim 24 in which the surface of instant claim 1 is part of an affinity purification matrix" (see Office Action mailed March 19, 2009, p. 13, 4th full para.). The Examiner relied on Brigstock for allegedly overcoming this

deficiency.

Brigstock teaches heparin-binding growth factor (HBGF) polypeptides as well as nucleic acids encoding the same and antibodies which bind to the HBGF polypeptides. Brigstock discloses the use of a heparin affinity chromatographic column in its purification of HBGF polypeptides. (P. 7, paras. [0060] to [0063]). However, no additional detail regarding such a heparin affinity chromatographic column is provided. With no details on whether or not the polypeptides are immobilized, Brigstock does not overcome the deficiencies noted above of Short, Mori, Hu and Keogh. It is respectfully submitted that claim 24 is patentable over Short, Mori, Hu, Keogh and Brigstock, each taken alone or in combination.

Claim 25 stands rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Short (Short *et al.* in WO 01/31339 A1; published May 3, 2001) in view of Mori (Mori *et al.* in U.S. Patent 5,053,398; published October 1, 1991), Hu (Hu *et al.* in U.S. Patent 4,865,870; published September 12, 1989) and Keogh (Keogh *et al.* in U.S. Patent 5,925,552; published July 10, 1999) as applied to claims 1-20 above, and further in view of Dukler (Dukler et al. in US 2002/0094541, published July 18, 2002). The Examiner admitted that the "Short, Mori, Hu and Keogh references do not teach the limitations of instant claim 24 [sic, 25] in which the surface of instant claim 1 is part of a microarray" (see Office Action mailed March 19, 2009, p. 15, 1st para.). The Examiner relied on Dukler for allegedly overcoming this deficiency.

Dukler teaches combinatorial complex libraries and methods for the manufacture of addressable complex carbohydrate microarrays as well as uses thereof. As the carbohydrate microarrays of Dukler are addressable, one of skill in the art would not be motivated to employ passive adsorption of carbohydrates to the substrate surface since such non-covalent bonds would be impractical to produce in an addressable format. Dukler states that, "the libraries according to

the present invention are preferably synthesized on a solid phase support. As such, the first building block is provided with a suitable functional group for binding such a support." (P. 15, para. [0165]). Furthermore, with respect to linking the first saccharide building block to the solid phase support, Dukler states, "The first saccharide building block is preferably covalently attached to the solid phase matrix via a single atom (e.g., the solid phase functional group) or a linker." (P. 15, para. [0154]). In fact, Dukler states, "... covalent immobilization methods enable the use of a very high ionic strength buffer (e.g., 6 M Guanidine HCl or 100 mM NaOH) in subsequent washing steps thus allowing accurate "in situ" verification of each enzymatic step utilized by the process. The removal of nonspecifically bound molecules is crucial for accurate library synthesis." (P. 49, paras. [0242] and [0243], first sentence). Thus, one of skill in the art reading Dukler would choose covalent attachment over non-covalent attachment of a carbohydrate to a surface of the microarray. Accordingly, Dukler does not overcome the deficiencies noted above of Short, Mori, Hu and Keogh. It is respectfully submitted that claim 25 is patentable over Short, Mori, Hu, Keogh and Dukler, each taken alone or in combination.

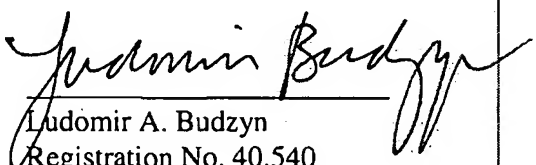
DOUBLE PATENTING REJECTION

Claims 1-3 and 21 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 48-53 of copending Application No. 11/269,427. Applicants point out that Application No. 11/269,427 has been abandoned for failure to respond to an Office Action. Thus, this rejection no longer applies and Applicants respectfully request withdrawal thereof.

CONCLUSION

Favorable action is earnestly solicited. If there are any questions or if additional information is required, the Examiner is respectfully requested to contact Applicants' attorney at the number listed below.

Respectfully submitted,



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